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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/702,149

11/04/2003

Robert L. Dow

PC25146A

7820

28523

7590

10/27/2006

PFIZER INC.

PATENT DEPARTMENT, MS8260-1611

EASTERN POINT ROAD

GROTON, CT 06340

EXAMINER

FREISTEIN, ANDREW B

ART UNIT

PAPER NUMBER

1626

DATE MAILED: 10/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/702,149

Applicant(s)

DOW ET AL.

Examiner

Andrew B. Freistein

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) 6-9 and 14-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12-13 is/are rejected.
- 7) ☒ Claim(s) 1-5 and 10-13 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 6) <input type="checkbox"/> Other: _____ |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date : 11/04/2003, 4/12/2004, 6/01/2004, 7/30/2004 and 12/15/2004.

DETAILED ACTION

Claims 1-23 are currently pending in the instant application.

Priority

This application claims benefit of US Provisional Application No. 60/432,911, filed 12/12/2002.

Information Disclosure Statement

Applicant's information disclosure statements (IDS), filed on 11/04/2003, 4/12/2004, 6/01/2004, 7/30/2004 and 12/15/2004 have been considered. Please refer to Applicant's copies of the 1449 submitted herewith.

Restriction Requirement

Applicant's election of Group I, claims 1-5 and 10-13 (in part), drawn to compounds and compositions classified in various subclasses of classes 514, 546 and 548, in the reply filed on 07/06/2006, is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

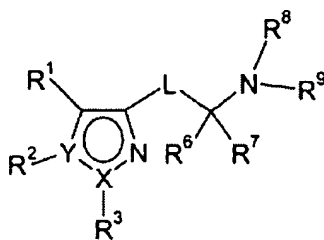
Status of the Claims

Claims 1-5 and 10-13 (in part) are withdrawn from further consideration by the Examiner as being drawn to non-elected inventions under 37 CFR § 1.142(b). The withdrawn subject matter is patentably distinct from the elected subject matter as it differs in structure and element and would require separate search considerations. In

addition, a reference that anticipates one invention would not render obvious the other invention.

Elected and Examined Subject Matter

The scope of the invention of the elected subject matter and the examined subject matter is as follows:



Compounds of the Formula (I), , wherein:

X, Y, R¹, R², R³, L, R⁴, R⁵, R⁶ and R⁷ are as defined in claim 1;

R⁸ is H, (C₁-C₆)alkyl,

-C(O)(CH₂)_mR¹⁰, -SO₂(CH₂)_nR¹⁰, or -(CH₂)_pR¹⁰, where m and n are 0, 1, or 2, p is 0, 1, 2 or 3, and R¹⁰ is selected from the group consisting of (C₁-C₈)alkyl, a partially or fully saturated cycloalkyl, aryl, heteroaryl, and a partially or fully saturated heterocycle, where said (C₁-C₈)alkyl, said cycloalkyl, said aryl, said heteroaryl and said heterocycle are optionally substituted with one or more substituents;

R⁹ is H, (C₁-C₆)alkyl,

-C(O)(CH₂)_mR¹⁰, -SO₂(CH₂)_nR¹⁰, or -(CH₂)_pR¹⁰, where m and n are 0, 1, or 2, p is 0, 1, 2 or 3, and R¹⁰ is selected from the group consisting of (C₁-C₈)alkyl, a partially or fully saturated cycloalkyl, aryl, heteroaryl, and a partially or fully saturated heterocycle, where said (C₁-C₈)alkyl, said cycloalkyl, said aryl, said heteroaryl and said heterocycle are optionally substituted with one or more substituents;

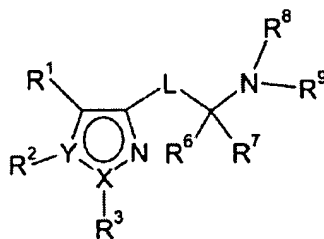
or

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R^8 and R^9 are taken together to form a partially or fully saturated 6-membered heterocyclic ring containing the N atom as the only heteroatom and optionally substituted with one or more substituents.

Non-elected and Non-examined Subject Matter

The scope of the invention of the non-elected and non-examined subject matter is as follows:



Compounds of the Formula (I), , wherein:

R^8 and R^9 are taken together to form a partially or fully saturated 4- to 5- or 7- to 8-membered heterocyclic ring containing 1 to 3 heteroatoms and optionally substituted with one or more substituents, or R^8 and R^9 are taken together to form a partially or fully saturated 6-membered heterocyclic ring containing 2 to 3 heteroatoms and optionally substituted with one or more substituents.

As a result of the election and the corresponding scope of the invention, identified supra, the remaining subject matter of Claims 1-5 and 10-13 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected inventions. The withdrawn compounds contain varying functional groups such as morpholine, piperazine, thiomorpholine, azepanyl, azetidine, etc. which are chemically recognized to differ in structure, function, and reactivity.

Therefore, the subject matter which was withdrawn from consideration as being non-elected subject matter materially differs in structure and composition from the

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elected/examined subject matter so that a reference which anticipates the elected/examined subject matter would not render obvious the non-elected subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pharmaceutical compositions comprising the compound of the formula I as found in claim 1 and additional therapeutic agents selected from a nicotine receptor partial agonist (e.g. bupropion hydrochloride), an opioid antagonist (e.g. naltrexone), a dopaminergic agent (e.g. apomorphine), an attention deficit disorder agent (e.g. methylphenidate hydrochloride), or an anti-obesity agent (e.g. orlistat), a monoamine reuptake inhibitor (e.g. sibutramine), a dopamine agonist (e.g. bromocriptine), a lipase inhibitor (e.g. tetrahydrolipstatin), and a ciliary neurotrophic factor (e.g. AxokineTM), the specification does not reasonably provide enablement for a pharmaceutical composition comprising the compound of the formula I as found in claim 1 and an anti-obesity agent selected from: an apo-B/MTP inhibitor, a 11 β -hydroxy steroid dehydrogenase-1 inhibitor, peptide YY₃₋₃₆ or an analog thereof, a MCR4 agonist, a CCK-A agonist, a sympathomimetic agent, a β_3 adrenergic receptor agonist, a melanocyte-stimulating hormone receptor analog, a 5-HT_{2c} receptor agonist, a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor

agonist, a galanin antagonist, a bombesin agonist, a neuropeptide-Y receptor antagonist, a thyromimetic agent, dehydroepiandrosterone or analog thereof, a glucocorticoid receptor antagonist, an orexin receptor antagonist, a glucagon-like peptide-1 receptor agonist, a human agouti-related protein antagonist, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or inverse agonist, and a neuromedin U receptor agonist.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

The nature of the invention is a pharmaceutical composition comprising the compound of the formula I as found in claim 1 and additional therapeutic agents selected from anti-obesity agents.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to pharmaceutical compositions comprising multiple active agents, one would need to consider drug-drug interactions.

For the preparation of pharmaceutical compositions containing multiple active ingredients, one needs to take into account drug-drug interactions. For example, there are various types of anti-obesity agents known in the prior art. Obach discloses that in regards to any given pharmacokinetic drug-drug interaction, the two drugs involved can

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be considered as either the “perpetrator” drug or the “victim” drug (see Obach, Drugs of Today 39(5), p. 301-338 (2003)). The perpetrator is the drug that affects the activity of an enzyme or protein involved in the metabolism or disposition of the victim drug. The victim drug is the one that either causes side-effects or toxicity due to increased exposure, or lack of efficacy due to exposure decreased to below that required for therapeutic effect (page 302). There are varying mechanisms of drug interactions such as the reduction in the rate of the metabolism of one drug by another, the irreversible inactivation of drug-metabolizing enzymes and the exposure to the victim drug is decreased (pages 303-304). Obach also discloses that there are a number of in vitro and in vivo experimental approaches to be taken to determine drug-drug interactions (page 304).

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present for the pharmaceutical compositions containing additional therapeutic agents in the instant specification is found on pages 33-36. Moreover, on page 34, the specification incorporates by reference 9 other publications as disclosing anti-obesity agents. The specification does disclose some examples of an anti-obesity agents (e.g. orlistat), the specification does not provide examples for all of the other inhibitors, agonists, antagonists, proteins, etc. that Applicant claims, nor does the specification disclose what the breadth of the term anti-obesity agent encompasses. Furthermore, there is no pharmaceutical composition

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actually prepared in the instant specification which contains any type of anti-obesity agent.

The breadth of the claims

The breadth of the claims is pharmaceutical compositions comprising the compound of the formula I as found in claim 1 and additional anti-obesity agent selected from an apo-B/MTP inhibitor, a 11 β -hydroxy steroid dehydrogenase-1 inhibitor, peptide YY.sub.3-36 or an analog thereof, a MCR4 agonist, a CCK-A agonist, a sympathomimetic agent, a β .sub.3 adrenergic receptor agonist, a melanocyte-stimulating hormone receptor analog, a 5-HT_{2c} receptor agonist, a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a bombesin agonist, a neuropeptide-Y receptor antagonist, a thyromimetic agent, dehydroepiandrosterone or analog thereof, a glucocorticoid receptor antagonist, an orexin receptor antagonist, a glucagon-like peptide-1 receptor agonist, a human agouti-related protein antagonist, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or inverse agonist, and a neuromedin U receptor agonist.

The quantity of experimentation needed and the level of the skill in the art

While the level of the skill in the pharmaceutical art is high, the quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what anti-obesity agents could be administered with applicants' instant formula I without any direction found in the specification as to what type of anti-obesity agents are considered, and the drug-drug interactions of these agents with the

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compound of the formula I. While the level of skill in the art is high, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compositions exhibit the desired pharmacological activity. Thus, the specification fails to provide sufficient support of pharmaceutical compositions of the formula I and an additional anti-obesity agent. As a result necessitating one of skill to perform an exhaustive search for which anti-obesity agents can be combined with the compound of the formula I without negative drug-drug interactions.

Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001, states, “a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”.

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which anti-obesity agents could be combined in a pharmaceutical composition with the compound of the formula I, with no assurance of success.

Claim Objections

(1) Claims 1-5 and 10-13 are objected to as being drawn to non-elected subject matter.

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(2) Claim 12 is objected to, because it depends on claim 10. Examiner presumes claim 12 should depend on claim 11, because claim 11 is drawn to a pharmaceutical composition and claim 10 is drawn to a compound.

Telephone Inquiry

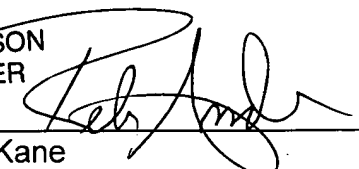
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew B. Freistein whose telephone number is (571) 272-8515. The examiner can normally be reached Monday-Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M^cKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Andrew B. Freistein
Patent Examiner, AU 1626

REBECCA ANDERSON
PATENT EXAMINER


Joseph K. M^cKane
Supervisory Patent Examiner, AU 1626
Date: October 26, 2006